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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/668,266	09/22/00	ROBISON K	35800/204489

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EXAMINER	
SISSON,B	
ART UNIT	**PAPER NUMBER**
1655	12

DATE MAILED: 08/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/668,266	Applicant(s) ROBISION ET AL.	
	Examiner Bradley L Sisson	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-43* is/are pending in the application.

4a) Of the above claim(s) *2-18,22,25,28,31,36,40,42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21,23,24,26,27,29,30,32-35,37-39,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Acknowledgement is made of applicant having filed an amendment whereby claim 1 was canceled and claims 19-43 have been added. Upon review of the newly added claims it has been noted that claims 19-21, 23, 24, 26, 27, 29, 30, 32-35, 37-39 and 41 most closely parallel the elected invention. Claims 2-18, 22, 25, 28, 31, 36, 40, 42, and 43 have been withdrawn from consideration as being drawn to inventions non-elected with traverse.

2. This application contains claims 2-18, 22, 25, 28, 31, 36, 40, 42, and 43 drawn to an invention nonelected with traverse in Paper No. 5. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26, 27, 29, 30, 32-35, 37-39, 41, and 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification has been found to set forth two deduced amino acid sequences: SEQ ID NO: 1 and SEQ ID NO: 3. The amino

acid sequences having been deduced from the nucleotide sequences set forth in SEQ ID NO: 2, and SEQ ID NO:4, respectively. It does not appear that any protein has actually been expressed, much less found to exhibit the anticipated phosphodiesterase activity. While support for variants and fragments can be found in the disclosure, e.g., pages 13 and 20, the suggestion that variants and fragments could be obtained does not reasonably suggest that applicant was in possession of same. At best, such statements provide motivation for others to identify such alternative sequences. The number of amino acid sequences encompassed by the claims is immense, yet the disclosure of but two deduced amino acid sequences is insufficient to support a position of having disclosed an adequate number of species encompassed by the claims. In support of this position, attention is again directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957); see pages 3-4 of Office action of 30 March 2001.

Acknowledgement is made of Applicant's argument at page 17 of the response received 05 July 2001, hereinafter the response, wherein it is asserted that the two species disclosed constitutes an representative number of species for demonstrating possession of the entire genus. This argument has been fully considered and has not been found persuasive. While the disclosure does set forth methods that could be used in the isolation and eventual identificaiton of alternative sequences, such method steps, as indicated in the prior Office action, constitute a product-by-process. Furthermore, they speak to the characteristics of the reagents used to isolated the claimed polypeptides, they do not describe the claimed protein. The situation at hand is analogous to that encountered in *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein is stated:

> In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed

> genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.
>
> Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

While the decision in *Lilly* involved claims to cDNA that encoded a protein, it is significant to note that the court held that "[t]he description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention." Applicant seemingly is arguing that by having described how the encoding nucleic acid is to perform, and suggesting possible sizes of the protein, and even giving the protein a name, is sufficient. Such descriptors, for reasons presented in the *en banc* decision in *Lilly* are not persuasive towards withdrawing the above rejection.

Claims 19-21, 23, 24, 26, 27, 29, 30, 32-35, 37-39, 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such

a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided

The amount of guidance provided is extremely limited, especially as it relates to the use of the claimed protein.

The Presence or Absence of Working Examples

While the specification has been found to contain prophetic statements of possible uses, there are no working examples provided. It is further noted that there is no evidence of record that the claimed polypeptide had actually been expressed and found to have the requisite activity. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue

experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').

*****

"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort

> to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the prior art has advanced to the point where the unpredictable nature of proteins is more commonly recognized. Further, the utilization of enzymes speaks to the application of simulated, if not actual chemical reactions and physiological activity- the very conditions that have been recognized by the Court as being highly unpredictable and requires a greater level of disclosure. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The Relative Skill of Those in the Art

> The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims encompass many thousands of proteins of varying amino acid composition, not all of which need have any activity, much less the activity associated with a phosphodiesterase. The only disclosed utility of the claimed protein is in its ability to act as a phosphodiesterase. The claims, however, are not limited to just those embodiments which

exhibit such activity. The specification is essentially silent as to how these non-enzymatic embodiments are to be used.

Even if the claims were to be limited to just those embodiments that have phosphodiesterase activity, the specification is silent as to how the claimed polypeptide is to be used in any particular assay. In short, the specification has not set forth the reaction conditions that are required for its use; see pages 6-7 of the prior Office action as it relates to the decision in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001.

Acknowledgement is made of applicant's assertions at page 20 of the response that the claims are enabled by the disclosure and that "one of skill in the art would be able to make and use the claimed invention with only the exercise of routine practices...." And where attention has bee directed to prior art publications incorporated into the subject specification. These arguments have been fully considered and have not been found persuasive.

With regard to the incorporation by reference of various journal articles, it appears that applicant is attempting to rely upon these non-patent publications for enablement. However, it is well settled that one cannot incorporate essential subject matter by reference especially when it is to be found in non-patent publications (U.S.). Further, applicant's remarks have not shown where the prior art teaches the use of the very proteins, fragments, and variants that are now being claimed, including those that lack any activity. Even if the does exist prior art that teaches the use of enzymes, applicant has not taught how these prior art methods/disclosures are to be adapted so to enable the use of the now claimed polypeptides. Accordingly, and in the absence of convincing evidence to the contrary, the rejection is newly applied against new claims .

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 29, 30, 32, and 33 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29, 30, 32, and 33 each recite a percent identity the claimed amino acid sequence is to have in relation to an identified SEQ ID NO. The claims, however, do not recite the algorithm used, and the values ascribed to the variables in the algorithm (e.g., Matrix, k-tuple, Mismatch Penalty, Joining Penalty, Randomization Group Length, Cutoff Score, Gap Penalty, Gap Size Penalty, Window Size or the length of the subject nucleotide sequence) such that the metes and bounds of the "percent identity" can be readily determined.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19-21, 23, 24, 26, 27, 37-39, 41 and 42 rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The invention of claims 19-21, 23, 24, 26, 27, 29, 30, 32-35, 37-39, 41 and 42 has been interpreted as encompassing polypeptides that have no activity and as such, no utility. In contrast, claim 29 is drawn to similar proteins that have phosphodiesterase activity. Accordingly, the above rejection can be overcome by amending the claims so to clearly

define the claimed protein as having phosphodiesterase activity- the only activity that has been asserted to be associated with some of the proteins.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephanie Zitomer can be reached on (703) 308-3985. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bradley L Sisson
Primary Examiner
Art Unit 1655

bls
August 16, 2001